Class 18: Pertussis Mini Project

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Background

Pertussis (aka whooping cough) is a common lung infection caused by the bacteria *B. Perussis*.

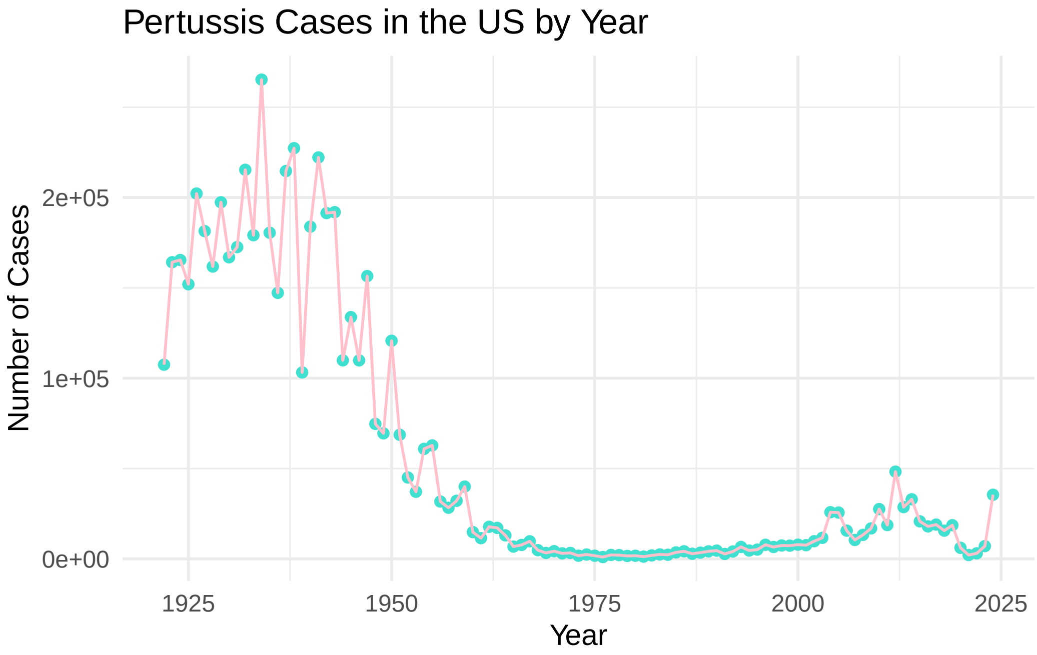
The CDC tracks cases of Pertussis in the US: https://tinyurl.com/pertussiscdc

Examining cases of Pertussis by year

We can use the **datapasta** package to scrape case numbers from the CDC website.

> Q. Make a plot of pertussis cases per year using ggplot.

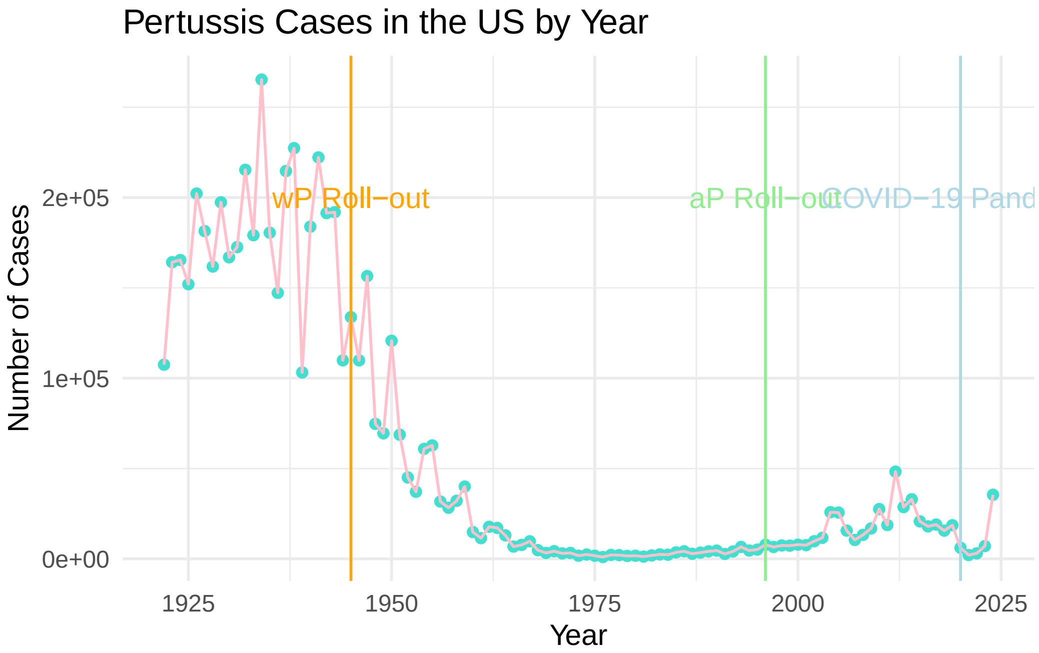
```r
library(ggplot2)

cases <- ggplot(cdc, aes(year, cases)) +
            geom_point(col="turquoise", alpha=2) +
            geom_line(col="pink") +
            labs(title = "Pertussis Cases in the US by Year",
                     x = "Year",
                     y = "Number of Cases") +
            theme_minimal()

cases
```



Q2. Add some key time points in our history of interaction with Pertussis to our plot. These include wP roll-out (the first vaccine) in 1945, and the switch to aP in 1996.

We can use `geom_vline()` for this.

```
cases +
  geom_vline(xintercept = 1945, col= "orange") +
  geom_vline(xintercept = 1996, col= "lightgreen") +
  geom_vline(xintercept = 2020, col= "lightblue") +
  annotate("text", x = 1945, y = 200000, label = "wP Roll-out", col= "orange") +
  annotate("text", x = 1996, y = 200000, label = "aP Roll-out", col= "lightgreen") +
  annotate("text", x = 2020, y = 200000, label = "COVID-19 Pandemic", col= "lightblue")
```



After the wP roll-out case numbers decreased significantly, and continued to stay low after the aP roll-out. In 2020, Covid pandemic began, and we see a significant decrease in cases, most likely due to quarentining, social distancing, and lockdown measures. However, in 2024, we see an increase in cases due to a variety of factors, such as vaccine hesitancy and vaccinations not being required for school.

Mounting evidence suggests that the **aP** vaccine is less effective over the long term than the older **wP** vaccine. Vaccine protection wanes more rapidly with the aP than with the wP, which is why a booster aP vaccine is required.

Enter the CMI-PB project

CMi-PB (computational models of Immunity - Pertusis boost) major goal is to investigate how the immune system responds differently with aP vs wP vaccinated individuals and be able to predict this at an early stage.

CMI-PB makes all their collected data freely available wnd theu store it in a database composed different tables. Here we will access a few of these.

We can use the **jsonlite** package to read this data.

```r
library(jsonlite)

subject <- read_json("https://www.cmi-pb.org/api/v5_1/subject", simplifyVector = TRUE)
```

```r
head(subject)
```

```
  subject_id infancy_vac biological_sex              ethnicity  race
1          1          wP         Female Not Hispanic or Latino White
2          2          wP         Female Not Hispanic or Latino White
3          3          wP         Female                Unknown White
4          4          wP           Male Not Hispanic or Latino Asian
5          5          wP           Male Not Hispanic or Latino Asian
6          6          wP         Female Not Hispanic or Latino White
  year_of_birth date_of_boost      dataset
1    1986-01-01    2016-09-12 2020_dataset
2    1968-01-01    2019-01-28 2020_dataset
3    1983-01-01    2016-10-10 2020_dataset
4    1988-01-01    2016-08-29 2020_dataset
5    1991-01-01    2016-08-29 2020_dataset
6    1988-01-01    2016-10-10 2020_dataset
```

> Q. How many subjects (i.e. enrolled people) are there in this dataset?

```r
nrow(subject)
```

```
[1] 172
```

> Q. How many "aP" and "wP" subjects are there?

```r
table(subject$infancy_vac)
```

```

aP wP 
87 85 
```

> Q. How many Male/Female are in the dataset?

```r
table(subject$biological_sex)
```

```

Female   Male 
   112     60 
```

> Q. How about gender and race numbers?

```
table(subject$race, subject$biological_sex)
```

```
                                               
                                                Female Male
  American Indian/Alaska Native                      0    1
  Asian                                             32   12
  Black or African American                          2    3
  More Than One Race                                15    4
  Native Hawaiian or Other Pacific Islander          1    1
  Unknown or Not Reported                           14    7
  White                                             48   32
```

> Q. Is this representative of the US population?

NO

Let's read another database table from the CMI-PB

```
specimen <- read_json("http://cmi-pb.org/api/v5_1/specimen", simplifyVector = TRUE)

ab_data <- read_json("http://cmi-pb.org/api/v5_1/plasma_ab_titer", simplifyVector = TRUE)
```

Take a peek

```
head(specimen)
```

```
  specimen_id subject_id actual_day_relative_to_boost
1           1          1                           -3
2           2          1                            1
3           3          1                            3
4           4          1                            7
5           5          1                           11
6           6          1                           32
  planned_day_relative_to_boost specimen_type visit
1                             0         Blood     1
2                             1         Blood     2
3                             3         Blood     3
4                             7         Blood     4
5                            14         Blood     5
6                            30         Blood     6
```

We want to “join” these tables to get all our information together. For this we will use **dplyr** package and the `inner_join()` function.

```
library(dplyr)
```

```

Attaching package: 'dplyr'

The following objects are masked from 'package:stats':

    filter, lag

The following objects are masked from 'package:base':

    intersect, setdiff, setequal, union
```

```
meta <- inner_join(subject, specimen)
```

```
Joining with `by = join_by(subject_id)`
```

```
head(meta)
```

```
  subject_id infancy_vac biological_sex              ethnicity  race
1          1          wP         Female Not Hispanic or Latino White
2          1          wP         Female Not Hispanic or Latino White
3          1          wP         Female Not Hispanic or Latino White
4          1          wP         Female Not Hispanic or Latino White
5          1          wP         Female Not Hispanic or Latino White
6          1          wP         Female Not Hispanic or Latino White
  year_of_birth date_of_boost      dataset specimen_id
1    1986-01-01    2016-09-12 2020_dataset           1
2    1986-01-01    2016-09-12 2020_dataset           2
3    1986-01-01    2016-09-12 2020_dataset           3
4    1986-01-01    2016-09-12 2020_dataset           4
5    1986-01-01    2016-09-12 2020_dataset           5
6    1986-01-01    2016-09-12 2020_dataset           6
  actual_day_relative_to_boost planned_day_relative_to_boost specimen_type
1                           -3                             0         Blood
2                            1                             1         Blood
3                            3                             3         Blood
```

```
4                            7                             7         Blood
5                           11                            14         Blood
6                           32                            30         Blood
  visit
1     1
2     2
3     3
4     4
5     5
6     6
```

```r
head(ab_data)
```

```
  specimen_id isotype is_antigen_specific antigen        MFI MFI_normalised
1           1     IgE               FALSE   Total 1110.21154       2.493425
2           1     IgE               FALSE   Total 2708.91616       2.493425
3           1     IgG                TRUE      PT   68.56614       3.736992
4           1     IgG                TRUE     PRN  332.12718       2.602350
5           1     IgG                TRUE     FHA 1887.12263      34.050956
6           1     IgE                TRUE     ACT    0.10000       1.000000
   unit lower_limit_of_detection
1 UG/ML                 2.096133
2 IU/ML                29.170000
3 IU/ML                 0.530000
4 IU/ML                 6.205949
5 IU/ML                 4.679535
6 IU/ML                 2.816431
```

One more “join” to get ab_data and meta all together.

```r
abdata <- inner_join(ab_data, meta)
```

```
Joining with `by = join_by(specimen_id)`
```

```r
head(abdata)
```

```
  specimen_id isotype is_antigen_specific antigen        MFI MFI_normalised
1           1     IgE               FALSE   Total 1110.21154       2.493425
2           1     IgE               FALSE   Total 2708.91616       2.493425
3           1     IgG                TRUE      PT   68.56614       3.736992
```

```
4           1     IgG                TRUE     PRN  332.12718       2.602350
5           1     IgG                TRUE     FHA 1887.12263      34.050956
6           1     IgE                TRUE     ACT    0.10000       1.000000
   unit lower_limit_of_detection subject_id infancy_vac biological_sex
1 UG/ML                 2.096133          1          wP         Female
2 IU/ML                29.170000          1          wP         Female
3 IU/ML                 0.530000          1          wP         Female
4 IU/ML                 6.205949          1          wP         Female
5 IU/ML                 4.679535          1          wP         Female
6 IU/ML                 2.816431          1          wP         Female
               ethnicity  race year_of_birth date_of_boost      dataset
1 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
2 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
3 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
4 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
5 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
6 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
  actual_day_relative_to_boost planned_day_relative_to_boost specimen_type
1                           -3                             0         Blood
2                           -3                             0         Blood
3                           -3                             0         Blood
4                           -3                             0         Blood
5                           -3                             0         Blood
6                           -3                             0         Blood
  visit
1     1
2     1
3     1
4     1
5     1
6     1
```

```r
dim(abdata)
```

```
[1] 61956    20
```

Q. How many Ab isotypes are there in the dataset?

```r
table(abdata$isotype)
```

```

  IgE   IgG  IgG1  IgG2  IgG3  IgG4 
 6698  7265 11993 12000 12000 12000 
```

Q. How many different antigens are measured in the dataset?

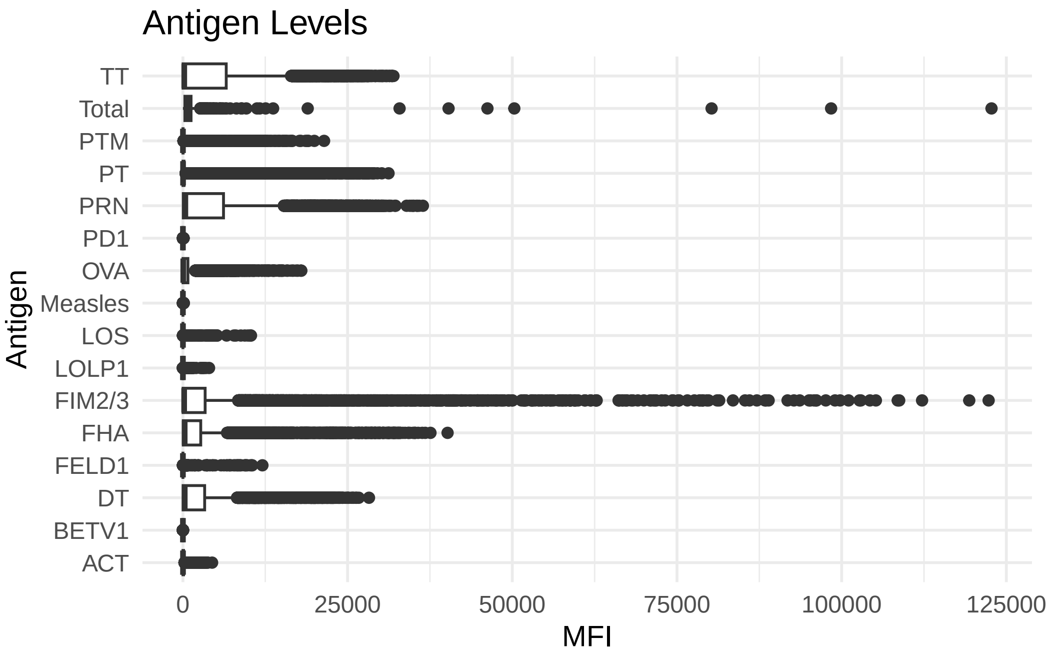
```
table(abdata$antigen)
```

```
    ACT   BETV1      DT   FELD1     FHA  FIM2/3   LOLP1     LOS Measles     OVA 
   1970    1970    6318    1970    6712    6318    1970    1970    1970    6318 
    PD1     PRN      PT     PTM   Total      TT 
   1970    6712    6712    1970     788    6318 
```

Q. Make a boxplot of antigen levels across the whole dataset (MFI vs antigen).

```
ggplot(abdata, aes(MFI, antigen)) +
  geom_boxplot() +
  labs(title = "Antigen Levels",
       x = "MFI",
       y = "Antigen") +
  theme_minimal()
```

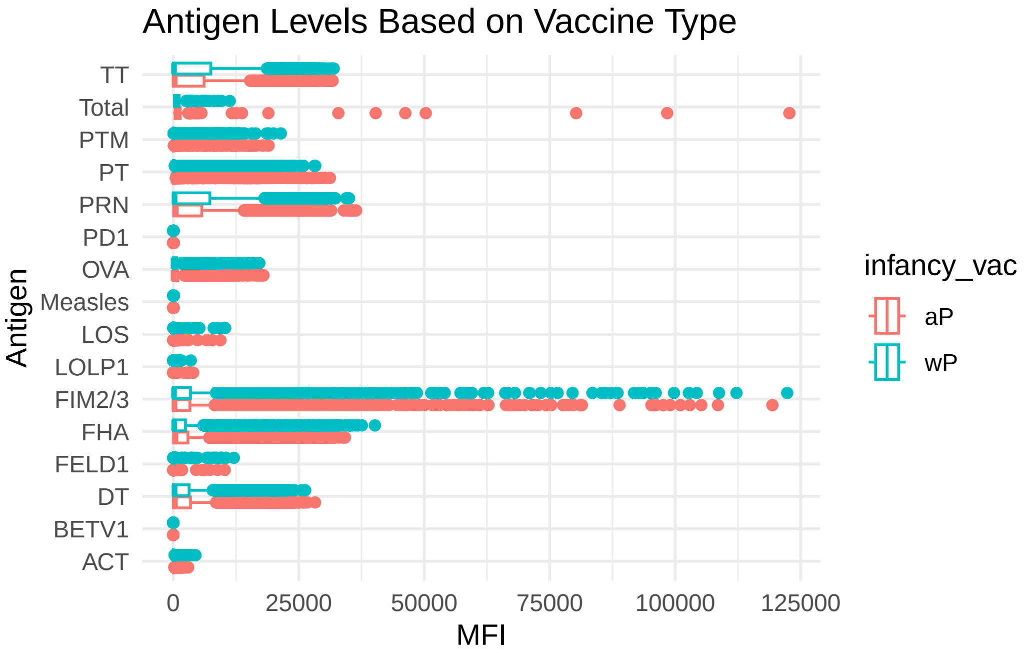
```
Warning: Removed 1 row containing non-finite outside the scale range
(`stat_boxplot()`).
```



Q. Are there obvious differences between aP and wP values

```r
ggplot(abdata) +
  aes(MFI, antigen, col=infancy_vac) +
  geom_boxplot() +
  labs(title = "Antigen Levels Based on Vaccine Type",
       x = "MFI",
       y = "Antigen") +
  theme_minimal()
```

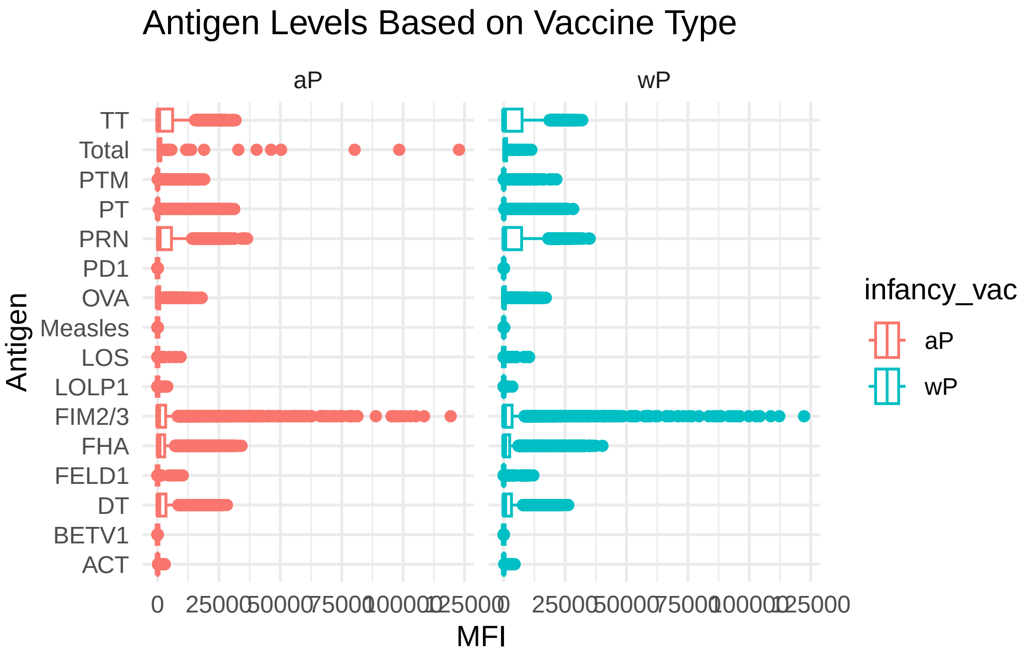
```
Warning: Removed 1 row containing non-finite outside the scale range
(`stat_boxplot()`).
```



Or we can "facet" by `infancy_vac` to get two individual plots one for each value of `infancy_vac`.

```r
ggplot(abdata) +
  aes(MFI, antigen, col=infancy_vac) +
  geom_boxplot() +
  facet_wrap(~infancy_vac) +
  labs(title = "Antigen Levels Based on Vaccine Type",
       x = "MFI",
       y = "Antigen") +
  theme_minimal()
```

```
Warning: Removed 1 row containing non-finite outside the scale range
(`stat_boxplot()`).
```



Focus on IgG levels

IgG is the most abundant antibidy in blood. With four sub-classes (IgG1, IgG2, IgG3, and IgG4) crucial for long-term immunity and responding to bacterial & viral infections.

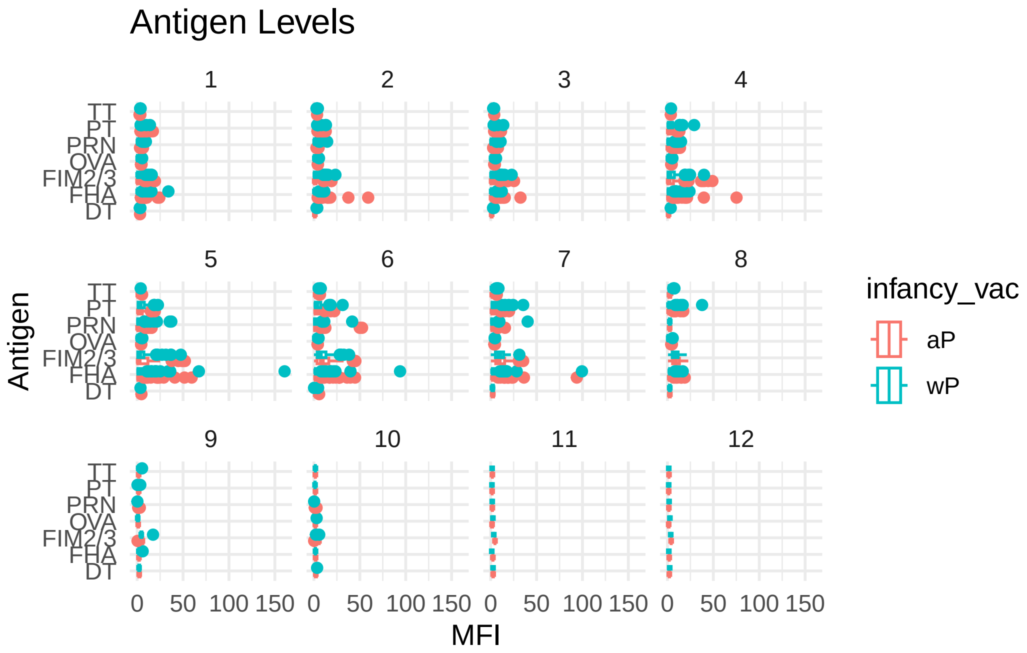
```
igg <- abdata |> filter(isotype=="IgG")

head(igg)
```

```
  specimen_id isotype is_antigen_specific antigen        MFI MFI_normalised
1           1     IgG                TRUE      PT   68.56614       3.736992
2           1     IgG                TRUE     PRN  332.12718       2.602350
3           1     IgG                TRUE     FHA 1887.12263      34.050956
4          19     IgG                TRUE      PT   20.11607       1.096366
```

```
5          19     IgG                TRUE     PRN  976.67419       7.652635
6          19     IgG                TRUE     FHA   60.76626       1.096457
   unit lower_limit_of_detection subject_id infancy_vac biological_sex
1 IU/ML                 0.530000          1          wP         Female
2 IU/ML                 6.205949          1          wP         Female
3 IU/ML                 4.679535          1          wP         Female
4 IU/ML                 0.530000          3          wP         Female
5 IU/ML                 6.205949          3          wP         Female
6 IU/ML                 4.679535          3          wP         Female
               ethnicity  race year_of_birth date_of_boost      dataset
1 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
2 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
3 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
4                Unknown White    1983-01-01    2016-10-10 2020_dataset
5                Unknown White    1983-01-01    2016-10-10 2020_dataset
6                Unknown White    1983-01-01    2016-10-10 2020_dataset
  actual_day_relative_to_boost planned_day_relative_to_boost specimen_type
1                           -3                             0         Blood
2                           -3                             0         Blood
3                           -3                             0         Blood
4                           -3                             0         Blood
5                           -3                             0         Blood
6                           -3                             0         Blood
  visit
1     1
2     1
3     1
4     1
5     1
6     1
```

Same boxplot as before but let's `facet_wrap()` by `visit` to see how antigen levels change over time.

```
ggplot(igg, aes(MFI_normalised, antigen, col=infancy_vac)) +
  geom_boxplot() +
  facet_wrap(~visit) +
  labs(title = "Antigen Levels",
       x = "MFI",
       y = "Antigen") +
  theme_minimal()
```



Focus in further on just one of these antigens - let's pick **PT** (Pertussis Toxin, one of the main toxins of the bacteria) in the **2021_dataset** again for **IgG** antibody isotypes.

```
table(igg$dataset)
```

```
2020_dataset 2021_dataset 2022_dataset 2023_dataset 
        1182         1617         1456         3010 
```

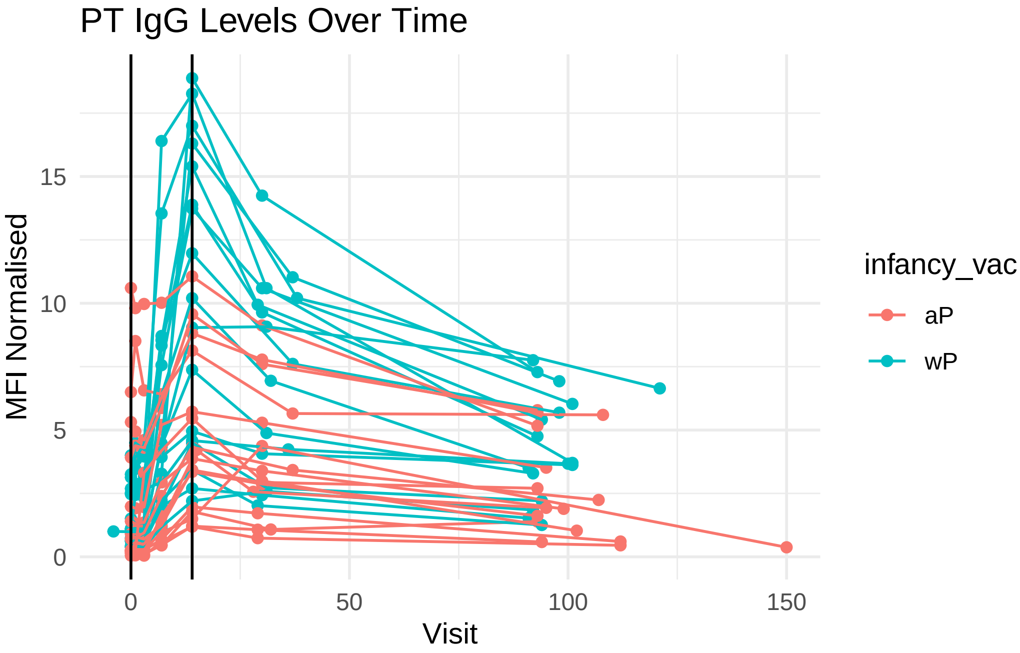
```
pt_igg <- abdata |> 
            filter(dataset=="2021_dataset",
                   antigen=="PT",
                   isotype=="IgG")
```

```
dim(pt_igg)
```

```
[1] 231  20
```

Let's make a plot of Time vs MFI_normalised.

```
ggplot(pt_igg) +
       aes(actual_day_relative_to_boost, MFI_normalised, col=infancy_vac, group=subject_id) +
  geom_point() +
  geom_line() +
  geom_vline(xintercept = 0) +
  geom_vline(xintercept = 14) +
  labs(title = "PT IgG Levels Over Time",
       x = "Visit",
       y = "MFI Normalised") +
  theme_minimal()
```


PT IgG Levels Over Time
MFI Normalised
Visit
infancy_vac
aP
wP